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EXAMINER	
SWITZER, JULIET CAROLINE	
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1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/803,858	LIEW, CHOONG-CHIN	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-43* is/are pending in the application.

4a) Of the above claim(s) *16,17,19-22 and 30-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15, 18, 23-29, 35, 37-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/18/08 has been entered.

2. Applicant's election without traverse of group II in the reply filed on 9/29/08 is acknowledged.

3. Elected claims 13-15, 18, 23-29, 35, and 37-43 are examined in their entirety or in part as in this office action, as indicated in the restriction requirement mailed 3/28/08. Linking claims 9-12 are also examined.

4. Applicant's amendments and remarks have been carefully considered but are not sufficient to place the claims in condition for allowance for the reasons set forth in this office action.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 13, 14, 23, 37, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Russell et al. (Blood, Vol. 84, No 4, 1994, pages 1243-1248).

Russell et al. teach a method for detecting expression of a zinc finger protein gene comprising detecting RNA encoded by said gene in a blood sample from a subject using RT-PCR (p. 1224). The gene encoding zinc finger protein detected by Russell et al. is the EVI1 gene. The RT-PCR method used by Russell et al. included the use of oligonucleotide primers specific for the RNA encoded by the zinc finger protein gene in the sample. Thus, Russell et al. teach a method meeting the limitations of claims 13, 14, 23.

Regarding claim 37, Russell et al. utilize a whole blood sample. Russell et al. further treat during analysis, and it is noted that the open claim language of the claim allows for additional steps within the scope of the method.

Regarding claim 39, the blood sample assayed by Russell et al. included mononuclear cells which includes the cell types listed in the claim.

7. Claims 13, 15, 18, 23-26, 37-41, and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Cocks et al. (6607879).

Cocks et al. teach methods for analyzing a sample using a collection of genes implicated in blood cell biology, and the collection includes a zinc finger protein (throughout; see SEQ ID NO: 243 in Table 1).

Cocks et al. teach a method for analyzing body fluid samples, including blood samples (Col. 10, lines 54-58), wherein RNA is isolated from the samples, the target polynucleotides are reverse transcribed into cDNA, a DNA is amplified from that cDNA (Col. 11, line 1 and following) and the cDNA is then hybridized to a collection of polynucleotides which include a

zinc finger protein (Col. 12-13 and throughout). Thus, Cocks et al. teach a method for detecting expression of a zinc finger protein in a human test subject comprising detecting RNA encoded by said gene in a blood sample of said test subject, using an oligonucleotide of predetermined sequence which is specific for RNA encoded by a zinc finger protein. (Claims 13, 23).

The method taught by Cocks et al. includes quantifying a level of RNA encoded by said gene in a sample (Col. 13, lines 4-25) and comparing said level of RNA to a quantified level of control (Col. 13, lines 11-20 and Col. 6 lines 54-65). Control subjects taught by Cocks et al. include healthy patients (Col. 6, beginning at line 55). (Claim 15, 18, 24, 25, 26, 43).

Cocks et al. teach quantifying relative to "normalization genes" which are housekeeping genes within the scope of the claim (see Col. 13).

Claims 37, 38, 39, 40, and 41 are rejected because Cocks et al. teach measuring expression in blood samples. In order to do so, a whole blood sample inherently would have to be taken from an individual. While Cocks et al. are silent as to how the RNA will be isolated or if the cells will be fractionated, the instant claims are drawn using "comprising" language and allow for additional manipulations of the whole blood sample which are not expressly set forth in the claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks et al. (US 6607879) in view of Chenchik et al. (US 5,994,076).

The teachings of Cocks et al. have been discussed previously in this office action.

Cocks et al. do not teach a method which includes producing an amplification product from RNA encoded by said gene using primers specific for only for RNA encoded by said gene and/or for cDNA complementary to RNA encoded by said gene.

However, at the time the invention was made, it was known to use gene specific primers to produce amplification products prior to hybridization with predefined arrays, as taught by Chenchik et al. (throughout; Col. 11).

It would have been prima facie obvious to one of ordinary skill in the art to have modified the invention taught by Cocks et al. so as to have used gene specific primers to amplify target sequences prior to hybridization with a microarray. In this case, all of the claimed elements were known in the prior art and one skilled in the art could have combined the known elements as claimed to provide a predictable result, namely the production of probe hybridization molecules particularly amplified to hybridize to the array taught by Cocks et al.

10. Claims 9, 10, 11, 37, 38, 41, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks et al. (US 6607879) in view of Sharma et al. (WO 98/49342) and Kruse et al. (Journal of Immunological Methods 210 (1997) pages 195-203).

Cocks et al. teach methods for analyzing a sample using a collection of genes implicated in blood cell biology, and the collection includes a zinc finger protein (throughout; see SEQ ID NO: 243 in Table 1). Cocks et al. teach that the microarray can be used to monitor disease and that researchers can assess and catalog the differences in gene expression between healthy and

diseased tissues or cells (Col. 14, beginning at line 23). Cocks et al. teach that the composition is particularly useful for diagnosing and monitoring the progression of diseases that are associated with blood cell biology including atherosclerois and myocardial inflammation (both heart diseases) (Col. 14, beginning at line 50).

Cocks et al. teach a method for analyzing body fluid samples, including blood samples (Col. 10, lines 54-58), wherein RNA is isolated from the samples, the target polynucleotides are reverse transcribed into cDNA, a DNA is amplified from that cDNA (Col. 11, line 1 and following) and the cDNA is then hybridized to a collection of polynucleotides (Col. 12-13 and throughout). Cocks et al. teach that differential hybridization experiments can be conducted to where two or more different biological samples are labeled with two or more fluorescent labels with different emission wavelengths (Col. 13).

The method taught by Cocks et al. includes quantifying a level of RNA encoded by said gene in a sample (Col. 13, lines 4-25) and comparing said level of RNA to a quantified level of control (Col. 13, lines 11-20 and Col. 6 lines 54-65). Control subjects taught by Cocks et al. include healthy patients (Col. 6, beginning at line 55). (Claim 15, 18, 24, 25, 26, 43).

Cocks et al. teach quantifying relative to "normalization genes" which are housekeeping genes within the scope of the claim (see Col. 13).

Cocks et al. do not particularly teach the use of blood samples that have not been fractionated into cell types.

Sharma et al. teach that from the very early stages of diseases the whole organism response to the changed condition (p. 10, 4th full ¶). In light of this, Sharma et al. teach a method for identifying a marker useful for diagnosing a disease comprising the steps of detecting

the presence of RNA in an unfractionated sample of whole blood from each of one or more subjects having said disease and quantifying a level of said RNA in said sample. Namely, Sharma et al. teach the preparation of gene transcript patterns beginning with extraction of mRNA from tissues, cells or body parts of an individual or organism which has a disease or condition (p. 7, final ¶, p. 12, 1st ¶), and particularly teach the isolation of total blood cell mRNA of blood samples which have not been fractionated into cell types (p. 35, section 5.1.1). Sharma et al. teach quantifying the level of expression and determining a difference between the quantified level in the sample from the diseased subject and a similarly quantified level of genes of control RNA from an unfractionated sample of whole blood from each of one or more first control subjects (p. 5, step (d); p. 15, first full ¶; p. 18, step (f); p. 11, final ¶).

In addition, at the time the invention was made, it was known that there were advantages in the analysis of mRNA expression in while blood samples. Kruse et al. teach these include that the preparation of RNA from whole blood much more resembles physiological conditions than RNA prepared from purified cells, that less material is required in comparison to some other methods, and that the possibility of storing blood for several months permits the analysis of multiple repetitive samples in parallel.

Thus, at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods of Cocks et al. so as to have screened whole blood samples for markers of atherosclerosis or myocardial inflammation, following the model of Sharma et al. Both Cocks et al. and Sharma et al. are concerned with the identification of markers for disease in the blood, and it would have been obvious to use the guidance of Sharma et al. to accomplish the task of identifying differentially expressed genes using the array

taught by Cocks et al. Further, one would have been motivated to use whole blood mRNA samples in particular by the express teachings of Kruse et al. as to motivations to use such a method. Regarding the requirement that the subject genes are genes that are expressed in blood and heart tissue of a subject not having said disease, this is considered to be an inherent property of at least some of the genes that would be detected by the methods taught by Cocks et al. in view of Sharma et al. and Kruse et al. Cocks et al. in view of Sharma et al. and Kruse et al. are a very similar method to that disclosed and claimed by applicant, and so the detected transcripts would be expected to identify genes expressed in blood and non-blood tissue of a subject not having said disease.

11. Claim 12 rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks in view of Sharma et al. and Kruse et al. as applied to claim 11 above, and further in view of Ralph et al. (WO 98/24935) or Ralph et al. (6190857).

The teaching of Cocks et al., Sharma et al., and Kruse et al. have been previously discussed in this office action. These do not provide a method which utilizes steps of producing amplification products using primers specific for only RNA encoded by the genes under analysis.

Ralph et al. carry out a differential display method to identify markers of disease in blood and then confirm the differential expression using RT-PCR. Namely, Ralph et al. teach that responses secondary to disease states may be reflected in changing patterns of leukocyte mRNA levels that correlate with the presence of the disease state (Col. 5, lines 27-33). Throughout, Ralph et al. teach a method of identifying differentially expressed markers using RNA fingerprinting, and the techniques used by Ralph et al. include amplification of mRNA using random primers and identifying differentially expressed molecules using gel electrophoresis.

Ralph et al. further explicitly teach that "frequently mRNAs identified by RNA fingerprinting or differential display as being differentially regulated turn out not to be so when examined by independent means. It is, therefore, critical that the differential expression of all mRNAs identified by RNA fingerprinting be confirmed as such by an independent methodology (paragraph bridging Col. 98-100)."

Ralph et al. exemplify this confirmation method in Example 5.6.2, beginning in column 98. Ralph et al. teach the use of RT-PCR to identify two or more markers useful for diagnosing a disease, namely prostate or breast cancer, exemplifying this method for the detection of two transcripts referred to by Ralph et al. as UC331 and UC332, these sequences are RNA encoded by each of two genes (Example 5.6.2 and following, Col. 98).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods taught by Cocks et al. in view of Sharma et al. and Kruse et al. so as to have included the RT-PCR step using oligonucleotides of predetermined sequence as taught by Ralph et al. so as to have provided a means to confirm the differential expression of the identified markers within a complete method of identifying two or more markers useful for diagnosing a disease.

12. Claims 13, 14, 15, 23, 24, 35, 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dai et al. (J Mol Cell Cardiol 30, 2365-2375 (1998)) in view of Campbell's Biology, Fourth Edition, page 821 (1996).

Dai et al. teach a method for detecting the expression of zinc finger protein in a sample using an oligonucleotide of predetermined sequence wherein detecting comprises producing an amplification product for RNA encoded by said gene in said blood sample from said test subject

using primer specific only for RNA encoded by said gene. Namely Dai et al. teach RT-PCR amplification of a zinc finger protein mRNA using primers identical to SEQ ID NO: 9 and SEQ ID NO: 10, page 2367. Further, Dai et al. teach quantifying the transcript with semiquantitative RT-PCR, page 2367. Dai et al. teach the analysis of expression in a variety of human tissue samples, page 2367 and figures 3 and 4. Dai et al. teach that a search of expression patterns of ZFPs in the cardiovascular system should provide important useful information.

Dai et al. do not teach a method wherein the sample is blood from a human subject.

At the time the invention was made, blood was known to also be a component of the cardiovascular system, as taught by Campbell. It would have been prima facie obvious to one of ordinary skill in the art to have expanded the samples for the tissue expression analysis to have included a human blood sample. One would have been so motivated in order to have provided an additional piece of information about the gene under study, especially since blood is a part of the cardiovascular system.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15. Claim 27 refers to "the comparison of step (c)." The claim is confusing because while the claim previously recites a step of comparing, it does not previously recite a step (c). Claim 28 is confusing for this same reason.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 41 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a rejection for new matter.

18. In claims 41 and 42, the limitation that the blood samples "comprises leukocytes which a have not been fractionated into cell types" is new matter. Such a recitation includes, for example, testing a blood sample where the red blood cells and the white blood cells have been separated, and also includes, the testing of whole blood RNA. There is clearly basis for the latter, but not the former.

19. Figure 5C shows standardized fractions of leukocytes. However, these are not leukocytes that have not been fractionated into cell types, as they have clearly been fractionated into cell types. While RNA levels have been determined in each of the fractions, this is not basis for the negative limitation "have not been fractionated into cell types." There is no discussion or example in the specification of the testing of RNA in blood samples which comprise leukocytes which have not been fractionated into cell types. Applicant has attempted to present a claim which excludes a particular process step from a method (that is, fractionating the leukocytes) and then provides basis for the exclusion of the step in a method where the opposite occurred. This

is not sufficient basis for the claim limitation because there is nothing in the specification that suggests applicant contemplated the exclusion of a step of fractionating leukocytes into cell types. Therefore, claims 41 and 42 are rejected for having new matter.

20. Claims 27, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of the invention

The rejected claims include steps of identifying a test subject as a candidate for having or being predisposed to heart failure or cardiac hypertrophy if it is observed that comparison of the individual's level of a zinc finger protein mRNA expression in blood is significantly higher than the level of expression in healthy control subjects.

Scope of the claims

The actual sequence of the gene whose expression to be detected is entirely unstated in the claims. The claims identify the gene only as "zinc finger protein" or "a ZFP gene." At the time the invention was made, there was no single molecule universally referred to as zinc finger protein. A "zinc finger" is a zinc-binding motif found in hundreds of different proteins throughout the genome. Laity et al. teach that zinc finger proteins are among the most abundant proteins in eukaryotic genomes, and that their functions are extraordinarily diverse (Laity et al, Current Opinion in Structural Biology 2001, 11:39-46). Thus, the scope of the claims is

extremely broad as to what gene's expression is measured and is used to suggest a predisposition or candidacy for heart failure or cardiac hypertrophy.

The claims recite comparing the level of RNA encoded by said gene in said sample to a quantified level of control RNA encoded by said gene in blood sample of healthy control subjects. The specification and claims are silent as to what the control level actually is.

Teachings in the Specification/Examples

The specification teaches that primers for ZFP, SEQ ID NO: 9 and SEQ ID NO: 10 were used and RT-PCR analysis was performed on a drop of blood. The specification teaches that ZFP expression was observed in the blood as well as differential expression levels of ZFP amongst normal, diabetic and asymptomatic preclinical diabetic subjects. The specification speculates that the higher expression levels of ZFP gene in their blood may indicate these subjects are headed in the "general direction" of cardiac hypertrophy and/or heart failure (¶0058 of US 2005/0196764, the pre-grant publication of the instant application).

The results are given in figure 5B. Here it appears that the highest level of expression was observed in "normal" individual 5C, and the lowest levels were observed in diabetic patient 6 and asymptomatic patient 7. There is no statistical analysis to determine if the differences could be considered not due to chance. Given the small sample sizes, overlap in expression observations and variability presented in the figures, it appears that the findings would not have been statistically different, and certainly would not support the conclusion that levels higher than healthy individuals indicates the presence of cardiac hypertrophy or heart failure.

The specification does not provide any data where cardiac hypertrophy patients or heart failure patients are tested.

State of the Prior Art and Level of Unpredictability

At the time the invention was made, it was known that expressed genes in whole blood could be indicative of some diseases, as noted in the prior art rejections in this office action.

It is unpredictable based on the data given in the specification if the relationships set forth in the rejected claims could ever be supported by data. No patients having the subject diseases have been tested, and the results based on diabetic patients are suggestive that at least some healthy patients have higher ZFP protein levels than individuals with diabetes.

Further, it is highly unpredictable, of all the possible proteins that are "zinc finger proteins" which ones would be predictive of or indicative of cardiac hypertrophy or cardiac failure.

Because the claims encompass any level of altered gene expression, it is relevant to point out that the post-filing art of Cheung et al (2003) teaches that there is natural variation in gene expression among different individuals. The reference teaches an assessment of natural variation of gene expression in lymphoblastoid cells in humans, and analyzes the variation of expression data among individuals and within individuals (replicates) (p.422, last paragraph; Fig 1). The data indicates that, for example, expression of ACTG2 in 35 individuals varied by a factor of 17; and that in expression of the 40 genes with the highest variance ratios, the highest and lowest values differed by a factor of 2.4 or greater (Fig 3). It is thus unpredictable as to whether or not any level of altered gene expression is indicative of a disease.

The unpredictability of correlating gene expression level to any phenotypic quality is taught in the post-filing art of Wu (2001). Wu teaches that gene expression data, such as microarray data, must be interpreted in the context of other biological knowledge, involving

various types of 'post genomics' informatics, including gene networks, gene pathways, and gene ontologies (p.53, left col.). The reference indicates that many factors may be influential to the outcome of data analysis, and teaches that expression data can be interpreted in many ways. The conclusions that can be drawn from a given set of data depend heavily on the particular choice of data analysis. Much of the data analysis depends on such low-level considerations as normalization and such basic assumptions as normality (p.63 - Discussion). The art of Newton et al (2001) further teaches the difficulty in applying gene expression results. Newton et al teaches that a basic statistical problem is determining when the measured differential expression is likely to reflect a real biological shift in gene expression, and replication of data is critical to validation (p.38, third full paragraph).

Quantity of Experimentation

The instant specification does not provide enabling support for the practice of a single embodiment within the claimed invention. The specification does not establish a reliable statistical relationship between any zinc finger protein expression levels in blood and cardiac hypertrophy or heart failure. The most data is provided with regard to diabetes, however, in this case, sample size is very small, and no analysis is performed to determine if the results are sufficiently predictive so as to rise to the level of differences in expression being sufficient to identify individuals as being candidates for or having a predisposition to disease. An extensive amount of work would be required to practice the claimed invention. Even for diabetes and patients with heart failure, although the specification suggests insulin and ZFP can be used for detection of these, no guidance is provided as to what level of differential expression is sufficient to make assignments as set forth in the claims. To practice the claimed invention one would

have to undertake substantial experimentation to determine that a predictive relationship exists, and commensurate in scope with the claims, this analysis would have to be undertaken for every gene that is broadly considered as a zinc finger protein.

In order to practice the claimed invention, one would have to undertake an extensive amount of experimentation in a highly unpredictable technology area. One would have to begin establishing using appropriate patients and controls which, if any zinc finger proteins, display differential expression in blood samples of individuals having heart failure or cardiac hypertrophy as compared to healthy individuals. One would also, have to carry out this testing for validation, for it is possible that the result observed in the instant specification is intrinsic to the very small cohort of patients evaluated in applicant's study. Further, one would have to undertake experimentation to determine difference thresholds required to determine that a patient has or does not have a disease. Each of these steps is highly unpredictable and success at observing the necessary relationship is not guaranteed.

Conclusion

The identification of gene differential expression/disease indication relationships is a highly unpredictable endeavor, requiring extensive experimentation. In light of the factors discussed, therefore, it is concluded that it would require undue experimentation to practice the claimed invention.

21. Claims 27, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of the claims is discussed previously in this office action. The claims require quantifying expression of a "zinc finger protein" gene. The proteins encoded by these genes are among the most abundant in eukaryotic genomes. Here, the assayed gene must be one that is differentially expressed in the blood of individuals that are candidates for or have a predisposition to developing heart failure or cardiac hypertrophy.

The specification does not provide actual evidence to support the assertion that a single one of these genes has the function required by the claims. The specification teaches primers for the amplification of a single ZFP (SEQ ID NO: 9 and SEQ ID NO: 10) but the specification does not provide data to support the asserted function. No correlation between the presence of a zinc binding motif and the requisite differential expression is disclosed. Those skilled in the art would not expect that any particular members of this extremely large genus mRNA would display the expression profile required to support the claimed invention.

The level of skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing which of those mRNA encoding proteins with zinc finger binding motifs would be useful within the claimed invention. Based on lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that the applicant was in possession of the claimed genus of methods.

Conclusion

22. No claim is allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Tuesday or Wednesday, from 9:00 AM until 4:30 PM, and Thursday afternoon from 12:30 PM until 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete

service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Juliet C. Switzer/
Primary Examiner
Art Unit 1634

January 14, 2009